	Hits	Search Text	DBs	Time Stamp
1	2179	fibroblast and 3T3	USPAT	2001/10/18 08:48
2	1250	l1 and (kill$ or cytotoxic or apoptosis or death)	USPAT	2001/10/18 08:49
3	1250	l1 and (kill$ or cytotoxic or apoptosis or death)	USPAT	2001/10/18 08:49
4	220	fibroblast with (kill$ or cytotoxic or apoptosis or death)	USPAT	2001/10/18 08:50
5	131	l4 and (freez$ or dry$ or $radiat$)	USPAT	2001/10/18 09:00
6	52	l5 and (extracellular matrix and adhesion)	USPAT	2001/10/18 09:10
7	13	l5 and (matrix and adhesion)	USPAT	2001/10/18 09:03
8	1092	matrix with cell with (growth or proliferation)	USPAT	2001/10/18 09:04
9	101	l8 and l2	USPAT	2001/10/18 09:09
10	450	fibroblast with (matrix or scaffold)	USPAT	2001/10/18 09:09
11	168	l10 and l8	USPAT	2001/10/18 09:09
12	104	l11 and (cytotoxic or death or kill$ or apoptosis)	USPAT	2001/10/18 09:10
13	41	l12 and ((matrix or scaffold) and adhesion and proliferation)	USPAT	2001/10/18 09:11

(FILE 'HOME' ENTERED AT 09:46:54 ON 18 OCT 2001)

FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 09:48:34 ON 18 OCT 2001

L1 22686 S FIBROBLAST AND (MATRIX OR SCAFFOLD)
L2 551 S L1 AND ADHESION AND PROLIFERATION
L3 56 S L2 AND (KILL OR CELL DEATH OR CYTOTOXIC OR APOPTOSIS)
L4 39 DUP REMOVE L3 (17 DUPLICATES REMOVED)
L5 5 S L4 AND 3T3

L5 ANSWER 1 OF 5 MEDLINE
ACCESSION NUMBER: 2000291563 MEDLINE
DOCUMENT NUMBER: 20291563 PubMed ID: 10828879
TITLE: Extinction of rac1 and Cdc42Hs signalling defines a novel p53-dependent apoptotic pathway.
AUTHOR: Lassus P; Roux P; Zugasti O; Philips A; Fort P; Hibner U
CORPORATE SOURCE: Institut de Genetique Moleculaire, CNRS UMR5535, IFR 24, 1919 Route de Mende, F-34293 Montpellier cedex 5, France.
SOURCE: ONCOGENE, (2000 May 11) 19 (20) 2377-85.
Journal code: ONC; 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000622
Last Updated on STN: 20000622
Entered Medline: 20000614

AB **Apoptosis** is a normal physiological process which eliminates cells that do not receive adequate extracellular signals. One of the pathways signalling **apoptosis** is controlled by the small GTPases of the Rho family, also involved in cell **proliferation**, differentiation and motility. Another major **apoptosis** signalling pathway involves the p53 tumour suppressor which is activated by a variety of stress and mediates growth arrest or **apoptosis** in normal cells. We show here that upon detachment from the extracellular **matrix**, **fibroblasts** undergo rapid **apoptosis** that can be rescued by constitutive activation of Rac1 and Cdc42Hs GTPases. Conversely, inhibition of Rac1 and Cdc42Hs efficiently triggers **apoptosis** in adherent cells. Interestingly, **apoptosis** is not observed in p53-/- cells either cultured in suspension or inhibited for Rac1 and Cdc42Hs activity. Moreover, Rac1 and Cdc42Hs extinction in normal cells activates endogenous p53. Using specific inhibitors of MAPK pathways, we demonstrate that, in our experimental system, p38 signals survival, while ERK activity is required for **apoptosis**. Our data constitute the first demonstration that Rac1 and Cdc42Hs control pathways that require simultaneous signalling through MAPK ERK and p53 to induce **apoptosis**.

L5 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 1999244945 MEDLINE
DOCUMENT NUMBER: 99244945 PubMed ID: 10226029
TITLE: Akt/PKB localisation and 3' phosphoinositide generation at sites of epithelial cell-**matrix** and cell-cell interaction.
AUTHOR: Watton S J; Downward J
CORPORATE SOURCE: Imperial Cancer Research Fund, 44 Lincoln's Inn Fields, London WC2A 3PX, UK.
SOURCE: CURRENT BIOLOGY, (1999 Apr 22) 9 (8) 433-6.
Journal code: B44; 9107782. ISSN: 0960-9822.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990614
Last Updated on STN: 20000303

Entered Medline: 19990601

AB Protein kinase B (PKB or Akt) is a mitogen-regulated protein kinase involved in the protection of cells from **apoptosis**, the promotion of cell **proliferation** and diverse metabolic responses [1]. Its activation is initiated by the binding of 3' phosphorylated phosphoinositide lipids to its pleckstrin homology (PH) domain, resulting in the induction of activating phosphorylation at residues Thr308 and Ser473 by upstream kinases such as phosphoinositide-dependent protein kinase-1 (PDK1) [2]. **Adhesion** of epithelial cells to extracellular **matrix** leads to protection from **apoptosis** via the activation of phosphoinositide (PI) 3-kinase and Akt/PKB through an unknown mechanism [3] [4]. Here, we use the localisation of Akt/PKB within the cell to probe the sites of induction of PI 3-kinase activity. In **fibroblasts**, immunofluorescence microscopy showed that endogenous Akt/PKB localised to membrane ruffles at the outer edge of the cell following mitogen treatment as did green fluorescent protein (GFP) fusions with full-length Akt/PKB or its PH domain alone. In epithelial cells, the PH domain of Akt/PKB localised to sites of cell-cell and cell-**matrix** contact, distinct from focal contacts, even in the absence of serum. As this localisation was disrupted by PI 3-kinase inhibitory drugs and by mutations that inhibit interaction with phosphoinositides, it is likely to represent the sites of constitutive 3' phosphoinositide generation that provide a cellular survival signal. We propose that the attachment-induced, PI-3-kinase-mediated survival signal in epithelial cells is generated not only by cell-**matrix** interaction but also by cell-cell interaction.

L5 ANSWER 3 OF 5 MEDLINE
ACCESSION NUMBER: 1999043868 MEDLINE
DOCUMENT NUMBER: 99043868 PubMed ID: 9822606
TITLE: Integrins induce activation of EGF receptor: role in MAP kinase induction and **adhesion**-dependent cell survival.
AUTHOR: Moro L; Venturino M; Bozzo C; Silengo L; Altruda F; Beguinot L; Tarone G; Defilippi P
CORPORATE SOURCE: Dipartimento di Scienze Mediche, Biochimica, Universita di Torino, Italy.
SOURCE: EMBO JOURNAL, (1998 Nov 16) 17 (22) 6622-32. Journal code: EMB; 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 20000303
Entered Medline: 19990113

AB **Adhesion** of human primary skin **fibroblasts** and ECV304 endothelial cells to immobilized **matrix** proteins, beta1 or alphav integrin antibodies stimulates tyrosine phosphorylation of the epidermal growth factor (EGF) receptor. This tyrosine phosphorylation is transiently induced, reaching maximal levels 30 min after **adhesion**, and it occurs in the absence of receptor ligands. Similar results were observed with EGF receptor-transfected NIH-**3T3** cells. Use of a kinase-negative EGF receptor mutant demonstrates that the integrin-stimulated tyrosine phosphorylation is due to activation of the receptor's intrinsic kinase activity. Integrin-mediated EGF receptor activation leads to Erk-1/MAP kinase induction, as shown by treatment with the specific inhibitor tyrphostin AG1478 and by expression of a dominant-negative EGF receptor mutant. EGF receptor and Erk-1/MAP kinase activation by integrins does not lead per se to cell **proliferation**, but is important for entry into S phase in response to EGF or serum. EGF

receptor activation is also required for extracellular **matrix** -mediated cell survival. **Adhesion**-dependent MAP kinase activation and survival are regulated through EGF receptor activation in cells expressing this molecule above a threshold level (5x10(3) receptors per cell). These results demonstrate that integrin-dependent EGF receptor activation is a novel signaling mechanism involved in cell survival and **proliferation** in response to extracellular **matrix**.

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:186434 CAPLUS
DOCUMENT NUMBER: 120:186434
TITLE: The amido black assay: a simple and quantitative multipurpose test of **adhesion**, **proliferation**, and cytotoxicity in microplate cultures of keratinocytes (HaCaT) and other cell types growing adherently or in suspension
AUTHOR(S): Schulz, Juergen; Dettlaff, Sabine; Fritzsche, Ute; Harms, Ute; Schiebel, Heike; Derer, Wolfgang; Fusenig, Norbert E.; Huelsen, Andrea; Boehm, Markus
CORPORATE SOURCE: Humboldt University of Berlin, Faculty of Medicine Charite, Institute of Biochemistry, Hessische Str. 3-4, Berlin, D-10115, Germany
SOURCE: J. Immunol. Methods (1994), 167(1-2), 1-13
CODEN: JIMMBG; ISSN: 0022-1759
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new multipurpose cell micro-assay has been developed, using the protein dye amido black 10B as an indicator of cell nos. in 96-well plates. The assay is reliable, rapidly performed and can be combined with morphol. evaluation and photog. of stained cells. It permits investigations of various cell types including the human keratinocyte line HaCaT and subclones, mouse **3T3 fibroblasts** and myeloma cells X63-Ag8.653. Briefly, cells are fixed by formaldehyde or glutaraldehyde and, following aspiration of fixative and non-adherent cells, are stained by amido black at pH 3.5. The protein-bound dye is completely eluted by NaOH and is scanned in a microplate reader at 620 nm against 405 nm or 750 nm. Non-adherent and semi-adherent cells are assayed by centrifugation of plates before fixation. The assay revealed a good linear correlation between absorbance of amido black, cell count and DNA content within the range 1000-64,000 HaCaT cells/well. The slope of the regression line varied with different cell types. Expts. with HaCaT cells and its c-Ha-ras oncogene-transfected subclones demonstrated the suitability of the assay for optimizing culture conditions, dose-response studies and for the screening and quantification of cell **adhesion** to extracellular **matrix** mols. The assay was also used to evaluate cytotoxicity of drugs such as hexadecylphosphocholine, target cell killing in co-cultures with interleukin-2-activated lymphocytes, and the testing of hybridoma antibodies for their biol. effects on **proliferation** and **adhesion**. The assay is highly reproducible, sensitive, independent of cellular aggregation and economical for multiple applications.

L5 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:474477 BIOSIS
DOCUMENT NUMBER: PREV199800474477
TITLE: Signaling by integrin receptors.
AUTHOR(S): Kumar, C. Chandra (1)
CORPORATE SOURCE: (1) Dep. Tumor Biol., Schering-Plough Res. Inst., 2015 Galloping Hill Road, Kenilworth, NJ 07033 USA

SOURCE: Oncogene, (Sept. 17, 1998) Vol. 17, No. 11, pp. 1365-1373.

ISSN: 0950-9232.

DOCUMENT TYPE: General Review

LANGUAGE: English

AB Adhesive interactions are critical for the **proliferation**, survival and function of all cells. Integrin receptors as the major family of **adhesion** receptors have been the focus of study for more than a decade. These studies have tremendously enhanced our understanding of the integrin-mediated adhesive interactions and have unraveled novel integrin functions in cell survival mechanisms and in the activation of divergent signaling pathways. The signals from integrin receptors are integrated from those originating from growth factor receptors in order to organize the cytoskeleton, stimulate cell **proliferation** and rescue cells from **matrix** detachment-induced programmed **cell death**. These functions are critical in the regulation of multiple processes such as tissue development, inflammation, angiogenesis, tumor cell growth and metastasis and programmed **cell death**.

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